"The Physiological Action of Choline and Neurine." By F. W. Mott, M.D., F.R.S., and W. D. Halliburton, M.D., F.R.S. Received March 13,—Read April 20, 1899.

(Abstract.)

The cerebro-spinal fluid removed from cases of brain atrophy, particularly from cases of General Paralysis of the Insane, produces when injected into the circulation of anæsthetised animals (dogs, cats, rabbits), a fall of arterial blood pressure, with little or no effect on respiration. This pathological fluid is richer in proteid matter than the normal fluid, and among the proteids, nucleo-proteid is present. The fall of blood pressure, is, however, due not to proteid, nor to inorganic constituents, but to an organic substance, which is soluble in alcohol. This substance is precipitable by phospho-tungstic acid, and by chemical methods was identified as choline. The crystals of the platinum double salt, which, when crystallised from 15 per cent. alcohol, are characteristic octahedra, form the most convenient test for the separation and identification of this base.

The nucleo-proteid and choline doubtless originate from the disintegration of the brain tissue, and their presence indicates that possibly some of the symptoms of General Paralysis may be due to auto-intoxication; these substances pass into the blood, for the cerebro-spinal fluid functions as the lymph of the central nervous system. We have identified choline in the blood removed by venesection from these patients during the convulsive seizures which form a prominent symptom in the disease.

Normal cerebro-spinal fluid does not contain nucleo-proteid or choline, or if these substances are present, their amount is so small that they cannot be identified. Normal cerebro-spinal fluid produces no effect on arterial pressure; neither does the alcoholic extract of normal blood or of ordinary dropsical effusions.

The presence of choline in the pathological fluids will not explain the symptoms of General Paralysis; for instance, it will not account for the fits just referred to. Its presence, however, is an indication that an acute disintegration of the cerebral tissues has occurred. If other poisonous substances are also present, they have still to be discovered.

Our proof that the toxic material we have specially worked with is choline, rests not only on chemical tests, but also on the evidence afforded by physiological experiments; the action of the cerebro-spinal substance exactly resembles that of choline. Neurine, an alkaloid closely related to choline, is not present in the fluid; its toxic action is much more powerful, and its effects differ considerably from those of choline.

Physiological Action of Choline.

The doses employed were from 1 to 10 c.c. of a 0·2 per cent. solution, either of choline or of its hydrochloride. These were injected intravenously.

The fall of blood pressure is in some measure due to its action on the heart, but is mainly produced by dilatation of the peripheral vessels, especially in the intestinal area. This was dmonstrated by the use of an intestinal oncometer. The limbs and kidneys are somewhat lessened in volume; this appears to be a passive effect, secondary to the fall in general blood pressure. The drug causes a marked contraction of the spleen, followed by an exaggeration of the normal curves, due to the alternate systole and diastole of that organ.

The action on the splanchnic vessels is due to the direct action of the base on the neuro-muscular mechanism of the blood vessels themselves; for after the influence of the central nervous system has been removed by section of the spinal cord, or of the splanchnic nerves, choline still causes the typical fall of blood pressure. The action of peripheral ganglia was in other experiments excluded by poisoning the animal previously with nicotine.

Section of the vagi produces no effect on the results of injecting choline.

We have obtained no evidence of any direct action of the base on the cerebral vessels.

Choline has little or no action on nerve trunks, as tested by their electrical response to stimulation. This aspect of the subject has been taken up by Dr. Waller and Miss Sowton, who will publish their results fully in a separate paper.

Choline has no effect on respiration.

The effect of choline soon passes off, and the blood pressure returns to its previous level. This is due partly to the great dilution of the substance injected by the whole volume of the blood, and may be partly due to the excretion of the alkaloid, or to its being broken up into simpler substances by metabolic processes. We could not find it in the urine.

If the animal has been previously anæsthetised with a mixture of morphine and atropine, the effect produced by choline is a rise of arterial pressure, accompanied by a rise of the lever of the intestinal oncometer. Other anæsthetics cause no change in the usual results. We consider this observation of some importance, for it shows how the action of one poison may be modified by the presence of another. This has some bearing on General Paralysis, for the arterial tension in that disease is usually high, not low, as it would be if choline were the only toxic agent at work.

Physiological Action of Neurine.

The doses employed varied from 1 to 5 c.c. of a 0·1 per cent. solution. These were injected intravenously.

Neurine produces a fall of arterial pressure, followed by a marked rise, and a subsequent fall to the normal level. Sometimes, especially with small doses, the preliminary fall may be absent. Sometimes, especially with large doses, by which presumably the heart is more profoundly affected, the rise is absent.

The effect of neurine on the heart of both frog and mammal is much more marked than is the case with choline; in the case of both choline and neurine, the action on the frog's heart is antagonised by atropine.

The slowing and weakening of the heart appear to account for the preliminary fall of blood pressure; in some cases this is apparently combined with a direct dilating influence on the peripheral vessels.

The rise of blood pressure which occurs after the fall, is due to the constriction of the peripheral vessels, evidence of which we have obtained by the use of oncometers for intestine, spleen, and kidney.

After the influence of the central nervous system has been removed by section of the spinal cord, or of the splanchnic nerves, neurine still produces its typical effects.

After, however, the action of peripheral ganglia has been cut off by the use of nicotine, neurine produces only a fall of blood pressure. It therefore appears that the constriction of the vessels is due to the action of the drug on the ganglia; in this, it would agree with nicotine, coniine, and piperidine.

Section of the vagi produces no influence on the results of injecting neurine.

In animals anæsthetised with morphine and atropine, injection of neurine causes only a rise of blood pressure, which is accompanied with constriction of peripheral vessels.

Neurine produces no direct results, so far as we could ascertain, on the cerebral blood vessels.

Neurine is intensely toxic to nerve-trunks (Dr. Waller and Miss Sowton).

It produces a marked effect on the respiration. This is first greatly increased, but with each successive dose the effect is less, and ultimately the respiration becomes weaker, and ceases altogether. The animal can still be kept alive by artificial respiration.

The exacerbation of respiratory movements will not account for the rise of arterial pressure; the two events are usually not synchronous, and an intense rise of arterial pressure (due, as previously stated, to contraction of peripheral blood vessels) may occur when there is little or no increase of respiratory activity or during artificial respiration.

As confirmatory of Cervello's statement that neurine acts like

curare on the nerve endings of voluntary muscle, and to which he attributes the cessation of respiration, we may mention that after an animal has been poisoned with neurine, asphyxiation causes little or none of the usual convulsions.

The full paper contains references to previous work on the subject, and complete details of the methods used, and the cases investigated; it is illustrated by reproductions of numerous tracings.

[*Note added April* 20, 1899.—It should be mentioned that in the cases of brain atrophy referred to, the cerebro-spinal fluid was removed soon after death. Since the foregoing abstract was written, we have, however, had the opportunity of examining two specimens removed during life by lumbar puncture, and the results of our experiments with these corroborate the conclusions previously arrived at.]

"On Intestinal Absorption, especially on the Absorption of Serum, Peptone, and Glucose." By E. WAYMOUTH REID, F.R.S., Professor of Physiology in University College, Dundee, St. Andrew's University, N.B. Received March 30,—Read April 20, 1899.

(Abstract.)

The experiments detailed in the full paper deal with the absorption from the intestine of the animal's own serum, and of solutions of glucose and peptone. The method employed has been that introduced by Leubuscher, in which two loops of intestine are simultaneously employed, the one the experimental, and the other the control, loop.

The conclusions arrived at are as follows:—

1. A physiological activity of the intestinal epithelium in the act of absorption is demonstrated by—

(*a*) The absorption by an animal of its own serum (or even plasma) under conditions in which filtration into blood capillaries or lacteals, osmosis, and adsorption are excluded.

(*b*) By the cessation or diminution of the absorption of serum when the epithelium is removed, injured, or poisoned, in spite of the fact that removal, at any rate, must increase the facilities for osmosis and filtration.

2. The activity of the cells is characterised by a slower uptake of the organic solids of the serum than of the water, and a rather quicker uptake of the salts than of the water. The relations to one another of the absorptions of these various constituents is variable in different regions of the intestinal canal (upper ileum, lower ileum, and colon).